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Salt taste enhancer compsn. contg. cationic surfactants - potentiating the taste of sodium chloride and helps regulate its intake

Patent Assignee: CENT INNOV TECHN (INNO-N)

Number of Countries: 002 Number of Patents: 006

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
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EP 305469	A	19890308	EP 88902658	A	19880210	198910
AU 8814843	A	19881010				198911
JP 3502517	W	19910613	JP 88502623	A	19880210	199130
EP 305469	A4	19901227	EP 88902658	A	19880210	199514
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Abstract (Basic): WO 8806850 A

A process for potentiating the sodium chloride taste in salted food or beverage contg. sodium chloride comprises adding to the food or beverage sodium chloride taste potentiating amts. of a cationic surfactant having the formula (I) where R1 = at least 11C aliphatic gp., R2, R3, R4 = 1-24C (alkyl, aryl, aralkyl, alkoxyalkyl), opt. at least 2 of R2, R3, R4 together form an aliphatic heterocyclic ring with quaternary N; X = mono or polyvalent anion of an acid; m = an integer equal to the valence of anion X; n = 1, y = 0, 1-12. A compsn. enhanced in sodium chloride taste consisting of sodium chloride or a food or beverage contg. the same and sodium chloride taste-potentiating amts. of at least one cationic surfactant of formula (I) is claimed. A process for reducing the sodium chloride content of a salted food or beverage contg. them comprises formulating a food or beverage with less than necessary amt. of sodium chloride to provide desired salty taste and adding a cationic surfactant of formula (I) in sufficient amts to potentiate the salt taste to reach the desired salty taste is claimed. A compsn. having enhanced salty taste contg. sodium chloride or a food or beverage contg. the same, a salty-tasting cpd. selected from a gp. consisting of cationic aminoacids and low mol.wt. dipeptides and salt taste-potentiating amts. of a cationic surfactant of formula (I) is claimed.

USE/ADVANTAGE - The compsn. provides a means for the potentiation in humans of the taste of sodium chloride which can be used to regulate its intake. The cpds. used in the compsn. are of low toxicity and are safe for human consumption.

Derwent Class: D13; E13

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<b>(21) International Application Number:</b> PCT/US88/00467 <b>(22) International Filing Date:</b> 10 February 1988 (10.02.88)  <b>(31) Priority Application Numbers:</b> 024,170 157,083  <b>(32) Priority Dates:</b> 10 March 1987 (10.03.87) 8 February 1988 (08.02.88)  <b>(33) Priority Country:</b> US  <b>(71) Applicant:</b> CENTER FOR INNOVATIVE TECHNOLOGY [US/US]; The Hallmark Building, Suite 201, 13873 Park Center Road, Herndon, VA 22071 (US).  <b>(72) Inventors:</b> DESIMORE, John, A. : 917 Hedgelawn Drive, Richmond, VA 23298 (US). HECK, Gerard, L. : 3410 Northridge Road, Richmond, VA 23235 (US).		<b>(74) Agent:</b> SARRO, Thomas, P.; Larson & Taylor, 727 S. 23rd Street, Arlington, VA 22202 (US).  <b>(81) Designated States:</b> AT (European patent), AU, BE (European patent), CH (European patent), DE (European patent), DK, FI, FR (European patent), GB (European patent), IT (European patent), JP, KR, LU (European patent), NL (European patent), NO, SE (European patent).  <b>Published</b> <i>With international search report.</i>
<b>(54) Title:</b> SALT TASTE ENHANCER  <b>(57) Abstract</b>  This invention relates to processes and compositions found useful for potentiating the taste of sodium chloride in humans. It has been found that the taste of sodium chloride can be enhanced in the human mouth by combining therewith or with foods or beverages containing same, small quantities of cationic surfactants comprised of certain quaternary ammonium salts. A preferred sodium chloride taste enhancing surfactant is cetyl pyridinium chloride.		

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SALT TASTE ENHANCER

This invention relates to cationic surfactants found useful for potentiating the taste of sodium chloride in humans.

BACKGROUND OF THE INVENTION

Sodium chloride, ordinary table salt, is an important component in many of the physiological processes of the human body. The chemical also imparts to foods a more palatable taste such that many foods are considered to be tasteless in the absence of salt. Unfortunately, it is also well known that there are diseases of the human body where the intake of salt in even ordinary amounts can adversely affect the control of that disease. In those instances, the intake of sodium chloride must be regulated. Hypertension and diabetes are examples of diseases where the regulation of sodium chloride intake is essential. For those individuals who must regulate their salt intake, they are presented with the difficult problem of how to flavor their food so as to make it palatable at low salt levels. Of the methods available for the regulation of the intake of sodium chloride, substituting potassium chloride for ordinary table salt is commonly used. But this and all other substitutes for sodium chloride are inadequate in that the taste of the substitute is usually perceived as different by the individual and there are frequently associated bitter aftertastes. Accordingly, a satisfactory substitute for sodium chloride is highly desirable.

Another approach to regulating the intake of sodium chloride is to reduce the intake level to one that can be accepted without injury to an individual's health. Investigators have been well aware that if the taste of low sodium chloride levels

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could somehow be enhanced, the related problems of regulating sodium chloride intake and maintaining food palatability would be solved. However, only recently has there been significant progress in understanding the physiology of salt taste perception vital to the investigation of salt taste enhancement. Research conducted by the inventors, in cooperation with others, to elucidate the physiology of taste perception recently resulted in a breakthrough by proving the existence of lingual sodium channels and the movement of sodium ions across the lingual tissue as a current, a discovery contra-indicated by then prevailing theory. This discovery was reported in Science, Vol. 214, pp. 1039-41, Nov. 27, 1981 which reference is incorporated herein in its entirety. Subsequent investigations by the inventors correlated their breakthrough with taste nerve response, which correlation has been independently verified by other investigators in the field. Soeda et al, Japanese Journal of Physiology, 35, 1101-1105 1981; S.A. Simon & J.L. Gavin, "Salt & Acid Studies on Canine Lingual Epithelium", 398-408, American, Physiological Society 1985.

In applying these discoveries to the investigation of salt taste enhancement, workers in the field have been searching for satisfactory compounds that increase sodium transport across lingual epithelium as a mechanism which would potentiate the taste of sodium chloride. Schiffman et al, "Bretylium Tosylate Enhances Salt Taste", Physiology & Behavior Vol. 36, 1129-1137 1986 reported that bretylium tosylate enhances salt taste in humans and rats as statistically determined in human taste tests and as measured from electrophysiological taste responses in rats.

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However, bretylium tosylate had no effect on the short circuit current in isolated dog lingual epithelium, apparently acting through other physiological pathways. Bretylium tosylate is (o-bromobenzyl) ethyldimethylammonium p-toluenesulfonate, an ethical drug dispensed for the treatment of serious coronary heart disease. It is an adrenergic blocking agent which exhibits toxic side effects. As a result, the drug is of doubtful use as a salt taste enhancer.

Tada et al, J. Agric Food Chem. 1984 32, 992-996 have reported on a group of polypeptides that exhibit a salty taste. It has been found that these compounds also exhibit a bitter component to that taste and, while they may possibly be used as a salt substitute, they have not been shown to potentiate salt taste.

Other problems faced by investigators in the development of salt taste potentiators include the requirement that the compound must be essentially non-reactive on the tongue except for the activity shown in taste enhancement; the compound must be chemically stable; it must be relatively non-toxic; it must be physically and chemically compatible with foods and beverages and; it must be economical.

#### OBJECTS OF THE INVENTION

It is an object of this invention to provide a process for the potentiation in humans of the taste of sodium chloride which can be used to regulate the intake of sodium chloride.

It is a further object of this invention to provide a process for the potentiation in humans of the taste of sodium chloride utilizing compounds or mixtures that are of low toxicity and safe for human consumption.

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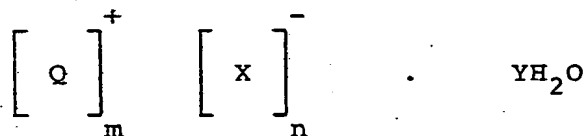
Yet a further object of this invention is to provide compositions and processes for the potentiation of the taste in humans of sodium chloride utilizing compounds, mixtures and methods that are compatible with ordinary foods and beverages and whose usefulness will not significantly deteriorate with time upon storage in admixture with such foods and beverages.

A further object of this invention is to provide a process that is economical, employing compounds or mixtures whose cost will not substantially affect the cost of the foods and beverages in which they are employed.

Another object of this invention is to provide a process for the enhancement of the taste in humans of sodium chloride employing compounds and mixtures that induce no secondary tastes which can be perceived by a human or that leave an after-taste other than that associated with the taste of sodium chloride.

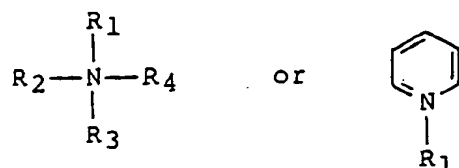
#### SUMMARY OF THE INVENTION

It has now been discovered that the taste of sodium chloride in humans can be potentiated by a process comprising applying to the taste surfaces in the mouth in conjunction with the intake of sodium chloride or a food or beverage containing sodium chloride, sodium chloride salt taste potentiating amounts of at least one cationic surfactant having the structure:



where Q is selected from the group comprising:

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wherein N is nitrogen;  $R_1$  is a saturated or unsaturated aliphatic group of at least eleven carbon atoms;  $R_2$ ,  $R_3$  and  $R_4$  are alkyl, aryl, aralkyl or alkoxyalkyl substituents of up to 24 carbon atoms, which substituents are alike or different, or where at least two of which collectively form an aliphatic heterocyclic ring with the quaternary nitrogen, X is a mono or polyvalent anion of an acid, m is an integer equal to the valence of the anion X; n is the integer 1, Y is O or an integer of 1 to 12.

In another aspect of the invention, a composition enhanced in salt taste is provided comprising sodium chloride or a food or beverage containing same in admixture with sodium chloride taste-potentiating amounts of the cationic surfactant described above.

#### DETAILED DESCRIPTION OF THE INVENTION

$R_1$  in the structure of the cationic surfactant of the invention may contain up to 24 carbon atoms and includes, for example, cetyl, lauryl, octadecyl, myristyl or like groups.

$R_2$ ,  $R_3$  and  $R_4$  can be any one of methyl, ethyl, propyl, butyl, pentyl, hexyl, octyl and their isomers, phenyl, tolyl, benzyl, anisyl, 2-phenylethyl, ethoxyethyl, methoxyethyl, cetyl, lauryl, octadecyl, myristyl, and the like. Examples of heterocyclic rings formed when two or more of  $R_2$ ,  $R_3$  and  $R_4$  are taken together with the N atom are piperidinium, morpholinium and octahydroindolizinium groups.



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The anion X in the cationic surfactant of the invention can be an anion of either a strong or a weak acid. Illustrations of suitable anions are chloride, bromide, fluoride, iodide, sulfate, nitrate, perchlorate, phosphate, trichloroacetate, paratoluene sulfonate, salicylate.

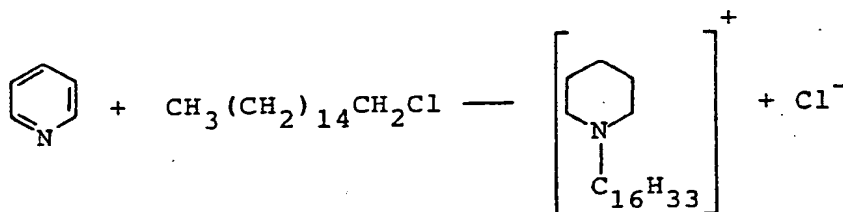
Thus, the cationic surfactants of the invention include, for example, cetylpyridinium chloride, cetylpyridinium sulfate, cetylpyridinium bromide, cetylpyridinium nitrate, cetylpyridinium paratoluene sulfate, laurylpyridinium chloride, laurylpyridinium sulfate, laurylpyridiniumtrichloroacetate, octadecylpyridinium chloride, octadecylpyridinium bromide, octadecylpyridinium sulfate, myristylpyridinium chloride, myristylpyridinium sulfate, myristylpyridinium nitrate, methylcetylpyperidinium chloride, methyl laurylpyperidinium sulfate, methyloctadecylpyperidinium chloride, ethylcetylpyperidinium chloride, hexyllaurylpyperidinium sulfate, butylmyristylpyperidinium chloride, diethylpyperidinium chloride, cetyl laurylpyperidinium chloride, methylcetylmorpholinium chloride, ethyllaurylmorpholinium chloride, benzylcetylmorpholinium bromide, ethoxyethylcetylmorpholinium chloride, cetyloctahydroindolizinium chloride, cetyltrimethylammonium chloride, phenylcetyldimethylammonium chloride, 2-phenylethylcetyldimethylammonium chloride, lauryltrimethyl ammonium chloride, laurylcetylmyristylmethylammonium chloride.

The preferred cationic surfactant for use in the invention is cetylpyridinium chloride, henceforth referred to herein as cpc. cpc is known to be a

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non-toxic, stable chemical compound, economical and readily compatible with foods and beverages.

The cationic surfactants employed in the present invention are prepared by methods well known in the art. In general, the methods are those commonly used for the preparation of quaternary ammonium compounds wherein a tertiary amine is contacted with an alkyl halide to produce the corresponding quaternary halide. For instance, cetylpyridinium chloride is prepared by the following reaction.



Those methods using aqueous reaction medium typically result in compounds containing one or more moles of water of hydration.

The cationic surfactants of the invention can be used singly or in combination to enhance salt taste perception. The concentration of the cationic surfactant necessary to enhance salt taste will vary depending principally upon the particular cationic surfactant employed. In general, the cationic surfactants of the invention can be used at very low concentrations; less than the critical micelle concentration of the surfactant, frequently this is 0.1 mM or less. The upper limit to the use of cpc would depend primarily on the development of an off taste in the foodstuff which may be associated with cpc at very high concentrations usually in excess of the critical micelle concentration where the surfactant would ordinarily not be used. Toxicity considerations would not limit the quantity of cpc

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which may be employed in a particular foodstuff preparation. The cationic surfactants may be added as a mixture with sodium chloride or separately to a previously salted foodstuff.

The usefulness of the cationic surfactants of the invention as enhancers of salt taste was discovered only after a protracted scientific investigation into the physiological events involved in salt taste perception in humans plus the development of scientific techniques to quantify the physiological events associated with such salt taste perception and correlation of those events with human salt taste response. In one method active ion transport across the canine lingual epithelium was studied using a short circuit current to investigate the type of chemical structures that enhanced sodium ion transport. Workers in the field have shown that increased current through sodium specific channels in the membrane of the tongue mucosa is an important event in salt taste transduction. Short circuit current measurement is a method used by investigators in this field to assess the increase current through sodium specific channels. The method is known to correlate well with human salt taste perception. The method can distinguish compounds that are known through other techniques to block sodium ion transport through the epithelium as well as respond in a quantitative way to experiments in sodium ion transport enhancement.

Using the short circuit current (SSC) method, cpc, when applied to the mucosa side of canine lingual epithelium increased the SSC several fold over baseline. In addition, the effect was found to be dose dependent. The enhancement is achieved at surprisingly low concentrations of cpc, ranging between 0.1mM to 1mM. Equally surprising, it was

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found that cpc not only increases the SSC, but also increases the sodium chloride current in post-treated tissues relative to pre-treated tissues.

The increases in SSC found through application of small concentrations of cpc, i.e., tenths millimolar, is unprecedented in the field. With cpc, the SSC has been shown to increase 280%.

That the increased short circuit current across canine lingual epithelium in the presence of cpc correlates with enhanced salt taste in humans was confirmed by taste tests described below.

Although it is not known for certain, it is believed that the long hydrocarbon chain represented by the  $R_1$  group in the cationic surfactant of the invention increases the solubility and membrane compatibility of the charged cation  $[2+]_m$  within sodium transport lingual channels increasing short circuit current and enhancing salt taste perception.

In light of the fact that the compounds of the present invention enhance salt taste perception in humans, it follows that the compounds of the present invention can be employed in combination with a salt such as sodium chloride or a salty-tasting substance such as arginine hydrochloride, in order to produce the perception of a saltier taste than would have been perceived from the salt or salty-tasting substance alone. This is useful because the perceived salt taste can be quantified by measuring the SSC for a given quantity of salt or the perceived salt taste may be quantified by measuring the neural response to the material as is demonstrated in Example 3. Then, a reduced amount of salt, or a salty-tasting substance or a mixture thereof, can be combined with the compounds of the present invention to produce the same SSC or neural response as the original, higher quantity of salt and therefore,

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produce the same perceived salt taste as that of the original higher quantity of salt. In this manner, the salt content of foods and beverages can be reduced by enhancing the perceived salt taste of the reduced quantity of salt with the compounds of the present invention to thereby produce the same perceived salt taste as would have been perceived had the original, higher quantity of salt been employed.

The salt taste enhancing compounds of the present invention may be employed to enhance the perceived salt taste of any salts used in food or beverage products. The preferred salt to be enhanced by the compounds of the present invention is sodium chloride primarily because of the recent discovery that ingestion of large amounts of sodium may have adverse effects on humans.

In addition, the compounds of the present invention may also be employed to enhance the perceived salt taste of known salty-tasting compounds which may be used as salt substitutes. Such compounds include cationic amino acids and low molecular weight dipeptides. Specific examples of these compounds are arginine hydrochloride, lysine hydrochloride and lysine-ornithine hydrochloride. These compounds exhibit a salty taste but are typically only useful in low concentrations since they exhibit a bitter flavor at higher concentrations. Ordinarily, these salty-tasting compounds will be used in amounts ranging from about 1 to about 40 millimolar concentrations, preferably from about 10 to about 30 millimolar concentrations. Thus, it is feasible to reduce the sodium chloride content of a food or beverage product by first formulating a food or beverage with less sodium chloride than is necessary to achieve a desired salt taste and then adding to said food or beverage the

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compounds of the present invention in an amount sufficient to potentiate the salt taste of said salted food or beverage to reach said desired taste. In addition, the sodium chloride content can be further reduced by substituting for a portion thereof, a salty-tasting cationic amino acid, low molecular weight dipeptide or mixtures thereof.

The following example is given to illustrate the short circuit current test procedure used in the evaluation of cpc as a salt taste enhancer. The procedure will be described with reference to the drawings wherein:

Fig. 1 is a side view of a Ussing chamber;

Fig. 2 is a graphical representation of the effect of cpc on short circuit current;

Fig. 3 is a graphical representation of increasing short circuit current in the presence of sodium chloride and cpc.

Fig. 4A, 4B & 4C show the results of neural recordings from the taste nerves of rats before and after treatment with cpc, as described in Example III.

#### EXAMPLE I

The detection of lingual epithelium short circuit current is conducted in a Ussing chamber. Referring to Fig. 1, the Ussing chamber consists of a Lucite block 1 partitioned into two chambers 2 and 3 by a tissue sample 4. Each chamber is filled with a buffer and oxygenated through tubes 5 and 6. The electrical potential difference across the tissue is monitored constantly using symmetrical calomel electrodes 7 and 8. Current passing electrodes 9 and 10 make contact with the buffer solutions. Stirrers 11 and 12, in cooperation with a heat source 13, and temperature sensor 14, maintain the chamber at

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constant temperature. The test tissue is the dorsal (top) epithelium of the tongue of a freshly killed dog mounted as a partition between the chambers with buffer solution bathing the mucosa or surface of the tongue as well as buffer separately in contact with the serosa side or interior surface of the tongue section. The tissue is bathed on both sides with the buffer solution and constantly gased with 95% oxygen and 5% carbon dioxide at a pH equaling 7.4. The electrical potential difference across the lingual epithelium is monitored constantly using symmetrical calomel electrodes which make contact with the buffer via 0.15 molar sodium chloride/agar salt bridges. The system is also fitted with Ag/AgCl current passing electrodes which make contact with the bathing solutions across the lingual epithelium also via salt bridges. In each case the system was allowed to develop a transepithelial electrical potential. After a steady state potential was achieved, the tissue was short circuited and the short circuit was continuously monitored on a strip chart recorder. To obtain the current response as a function of cpc concentration, the mucosa or oral cavity side solution is replaced by a solution of buffer containing a concentration of cpc. The time course of the change is followed and the system is allowed to achieve a new steady state.

Figure 2 is a dose response relationship for cpc in the buffer solution. Readily measurable increases in short circuit current occur between 0.1 millimolar and about 1 millimolar in buffer solution. The curve is sigmoidal, suggesting positive cooperativity in the activation of the current. In this case, the shape suggests that cpc must cross a diffusion barrier before it reaches its place of action. The shape supports a conclusion that a minimum

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concentration of cpc must be reached at its place of action before a significant increase in current can occur. Because the tissues were short circuited and were between identical reservoirs, except for the low concentration of cpc, the increase in current must ultimately be viewed as increased active current, i.e., metabolically linked current. The actual short circuit current was increased by approximately 280% due to cpc. Table 1 further illustrates the results of the experiment showing increased short circuit current due to cpc.

Table I

<u>cpc Concentration (mM)</u>	<u>Response (<math>\mu</math>A/sq.cm.) (Mean of Four Experiments)</u>	<u>Percent Increase</u>
0.0	28.4	
0.1	27.1	-4.80%
0.2	31.9	12.32%
0.4	56.6	99.30%
0.6	80.9	184.86%
0.8	96.1	238.38%
1.0	89.4	214.79%

The effect of cpc on the short circuit current at various concentrations of sodium chloride is presented in Figure III and in tabular form in Table II.

Table II

Effect of 0.5 mM cpc Treatment on salt response

<u>NaCl Concentration</u>	<u>Before</u>	<u>After</u>	<u>% Increase</u>
0.075M	14.5	16.3 $\mu$ A/Sq cm	12.41
0.15M	24.0	32.1	33.75
0.5M	124.3	248.6	100.00

These studies show that cpc causes the current to increase in response to sodium chloride solutions to a greater extent than in controls. In Fig. 3 control



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responses to 0.075 molar sodium chloride and 0.15 molar sodium chloride were obtained from a base line of 0.03 molar sodium chloride. After returning to base line in 0.03 molar sodium chloride the solution was changed to 0.03 molar sodium chloride containing 0.5 millimolar of cpc. The result is a slowly rising base line. When retested with 0.075 molar sodium chloride and 0.15 molar sodium chloride, the current responses were significantly increased over the controls. This effect is considerably greater at hyperosmotic sodium chloride concentrations. In Table II these same results are presented and show that, for example, before and after treatment with 0.5 millimolar cpc the current in 0.5 molar sodium chloride increases from 124.3 micro amps per square centimeter to 248.6 micro amps per square centimeter or a percent increase of 100%.

Based on the experience in the field in the correlation between short circuit current and the neural, or taste nerve response to sodium chloride the measure of the short circuit current and its increase in the presence of cpc is found to be a firm index for enhanced salt taste perception. The following example supports this conclusion.

#### EXAMPLE II

The following is a protocol suitable for demonstrating the salt taste enhancing character of cpc in humans.

1. Make up 0.15 M NaCl
2. Dissolve 2 mg of cpc in 100 ml of distilled water. (This gives a concentration of  $5.9 \times 10^{-5}$  M.)
3. Rinse mouth out with 10 ml of distilled water for 10 sec. Spit out water.

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4. Rinse whole mouth out with 10 ml 0.15 M NaCl for 10 sec. Note degree of saltiness and the rate of adaptation of the taste. Spit out solution.
5. Rinse whole mouth out with 10 ml of cpc solution for 10 sec. Cover the entire oral cavity including front and back of tongue. Spit out solution.
6. Rinse whole mouth out with 10 ml of 0.15 M NaCl for 10 sec. Note again the degree of saltiness and the rate of adaptation. Spit out solution. Note persistence of the saltiness even after the NaCl is expectorated. This prolongation of the salty experience often carries over to the next trial. In other words the saltiness adapts more slowly following cpc.
7. Repeat series several times.

It is found that the NaCl solution following cpc tastes saltier and that the saltiness adapts more slowly.

#### EXAMPLE III

In an attempt to find a neurophysiological model for the salt taste enhancing capacity of cpc, recordings have been made directly from the taste nerves of rats. Using conventional surgical methods the chorda tympany nerve, which innervates the anterior two-thirds of the tongue, was exposed and standard electrophysiological techniques were used to record the neural activity when sodium chloride was flowed over the tongue through a flow chamber affixed to the tongue surface. The responses to a sodium chloride stimulus were compared before and after treating the rat tongue with solutions of cpc at several concentrations. In general the effect of cpc

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was to increase the response of the taste nerves to a sodium chloride stimulus. Following cpc treatment the neural response to sodium chloride did not adapt as fast as the pretreatment controls. This is entirely consistent with the experience of human subjects wherein the sensation of "saltiness" appears more persistent following cpc than in the control case (cf Example II).

The results of the neural recording are shown in Figure 4. Figure 4A shows the integrated neural record in two cases (a and b). In each case the tongue was first adapted to 0.01 M NaCl. At the arrow on the left the adapting solution was displaced by 0.3 M NaCl. Case a shows the control response. This is the classical rapid increase in neural activity followed by a slow decrease in neural activity or adaptation. Case b shows the response to the same NaCl stimulus following  $5.9 \times 10^{-5}$  M cpc for 5 min. Note that adaptation is significantly slower, i.e. the neural response to NaCl remains higher than the control. The percent increase in neural activity following cpc is about 33%. Figure 4B shows a similar experiment using  $2.5 \times 10^{-4}$  M cpc. Again curve a is the control and curve b the response following cpc treatment. In this case the percent increased response following cpc treatment was about 45%. Figure 4C compares the rate of adaptation in the neural response to 0.3 M NaCl for three concentrations of cpc. Curve a corresponds to 0 cpc, curve b to  $5.9 \times 10^{-5}$  M cpc, and curve c to  $2.5 \times 10^{-4}$  M cpc. The rate of adaptation is either slowed or reversed by cpc.

Thus, as shown in Examples I, II and III, the salt taste enhancing ability of cpc can be documented as: 1) an increased salt-evoked current across the canine lingual epithelium in vitro, 2) increased

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human perception of saltiness, and 3) increased activity in the taste nerves of the rat in vivo.

#### EXAMPLE IV

Two cans of Campbell's low sodium tomato soup were opened and sufficient sodium chloride was added to produce a 50 millimolar sodium chloride concentration in the soups. To one can of the soup was added sufficient cpc to produce a 60 micromolar cpc concentration in the soup. Both soups were tasted by a panel of scientists and the soup including the cpc was found to have a stronger perceived salt taste which was equivalent to tomato soup having a 75-80 millimolar concentration of sodium chloride without cpc. From this it was concluded that a soup having 75-80 millimolar concentration of sodium chloride can be replaced by a soup having a 50 millimolar concentration of sodium chloride in combination with a 60 micromolar concentration of cpc to thereby reduce the sodium chloride content of the tomato soup without adversely affecting the saltiness.

#### EXAMPLE V

A 20 millimolar solution of arginine hydrochloride was prepared and tasted. It was found to be slightly salty. Then, sufficient cpc was added to the arginine hydrochloride solution to produce a 50 micromolar solution of cpc. The solution was tasted again and found to have a saltier taste than the original 20 millimolar solution of arginine hydrochloride.

#### EXAMPLE VI

A large pot of homemade chicken broth was prepared having a 50 millimolar sodium chloride

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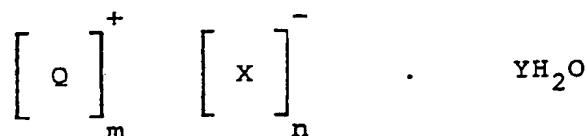
concentration. The soup was divided into two portions. One portion was left alone. To the second portion was added sufficient arginine hydrochloride to produce a 20 millimolar arginine hydrochloride solution. Also added to the second portion was sufficient cpc to produce a 50 micromolar solution of cpc. Both portions were tasted by a panel of scientists and the second portion was markedly saltier and tasted as salty as homemade chicken broth having a 100-150 millimolar sodium chloride concentration. From this it was concluded that the sodium chloride concentration can be further reduced by substituting arginine hydrochloride for a portion of the sodium chloride and employing a compound of the present invention to enhance the sodium chloride-arginine hydrochloride combination.

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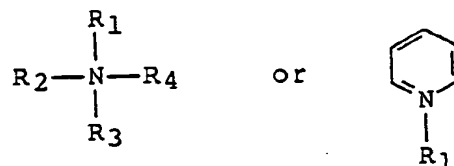
WHAT IS CLAIMED IS:

1. A process for potentiating the sodium chloride taste in a salted food or beverage containing sodium chloride comprising:

adding to said sodium chloride-containing food or beverage sodium chloride taste potentiating amounts of a cationic surfactant having the structure:



where Q is selected from the group comprising:



wherein N is nitrogen;  $\text{R}_1$  is a saturated or unsaturated aliphatic group of at least 11 carbon atoms;  $\text{R}_2$ ,  $\text{R}_3$  and  $\text{R}_4$  are alkyl, aryl, aralkyl or alkoxyalkyl substituents of up to 24 carbon atoms, which substituents are alike or different, or where at least two of which collectively form an aliphatic heterocyclic ring with quaternary nitrogen; X is a mono or polyvalent anion of an acid; m is an integer equal to the valence of the anion X; n is the integer 1; y is 0 or an integer of 1 to 12.

2. A process according to claim 1 wherein X is an anion of a strong acid.

3. A process according to claim 1 wherein X is an anion selected from the group consisting of chloride, bromide, fluoride, iodide, sulfate, nitrate and perchlorate.

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4. A process according to claim 1 wherein X is an anion of an organic acid.

5. A process according to claim 4 wherein the organic acid anion is paratoluene sulfonate.

6. A process according to claim 1 wherein  $R_1$  is selected from the group consisting of cetyl, lauryl, octadecyl or myristyl.

7. A process according to claim 1 wherein  $R_2$ ,  $R_3$  or  $R_4$  is taken from the group consisting of methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, and their isomers, phenyl, tolyl, benzyl, anisyl, 2-phenylethyl, ethoxyethyl.

8. A process according to claim 1 wherein the said cationic surfactant is cetyltrimethylammonium chloride.

9. A process according to claim 1 wherein the said cationic surfactant is cetyllauryldimethylammonium chloride.

10. A process according to claim 1 wherein  $R_2$ , and  $R_3$  collectively form a piperidinium group with nitrogen.

11. A process according to claim 1 wherein  $R_2$  and  $R_3$  collectively form a morpholinium group with nitrogen.

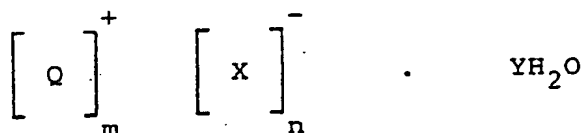
12. A process according to claim 1 wherein the said surfactant is cetylpyridinium chloride.

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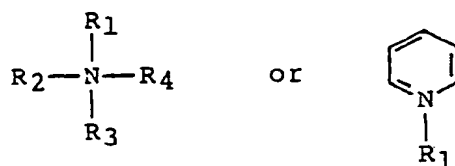
13. A process according to claim 1 wherein the said cationic surfactant is methylcetylpyperidinium chloride.

14. A process according to claim 1 wherein the said cationic surfactant is dicytylpyperidinium chloride.

15. A composition, enhanced in sodium chloride taste consisting essentially of sodium chloride or a food or beverage containing same and sodium chloride taste-potentiating amounts of at least one cationic surfactant having the structure:



where Q is selected from the group comprising:



wherein N is nitrogen;  $R_1$  is a saturated or unsaturated aliphatic group of at least eleven carbon atoms;  $R_2$ ,  $R_3$  and  $R_4$  are alkyl, aryl, aralkyl or alkoxyalkyl substituents of up to 24 atoms, which substituents are alike or different, or where at least two of which collectively form an aliphatic heterocyclic ring with quaternary nitrogen, X is a mono or polyvalent anion of an acid, m is an integer equal to the valence of the anion X; n is the integer 1, y is an integer of 1 to 12.



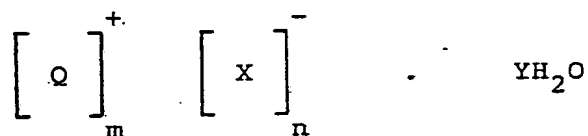
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16. A composition according to claim 15 wherein the cationic surfactant is cetylpyridinium chloride.

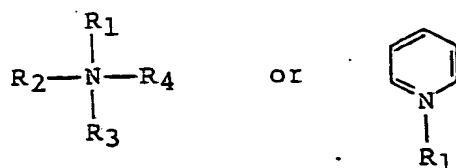
17. A process for reducing the sodium chloride content of a salted food or beverage containing sodium chloride comprising:

formulating a food or beverage with less sodium chloride than is necessary to achieve a desired salt taste in said food or beverage; and

adding to said sodium chloride-containing food or beverage a cationic surfactant in an amount sufficient to potentiate the salt taste of said salted food or beverage to reach said desired salt taste, said cationic surfactant having the structure:



where Q is selected from the group comprising:



wherein N is nitrogen;  $\text{R}_1$  is a saturated or unsaturated aliphatic group of at least 11 carbon atoms;  $\text{R}_2$ ,  $\text{R}_3$  and  $\text{R}_4$  are alkyl, aryl, aralkyl or alkoxyalkyl substituents of up to 24 carbon atoms, which substituents are alike or different, or where at least two of which collectively form an aliphatic heterocyclic ring with quaternary nitrogen; X is a mono or polyvalent anion of an acid; m is an integer equal to the valence of the anion X; n is the integer 1; y is 0 or an integer of 1 to 12.

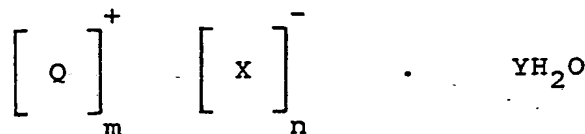
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18. A process in accordance with Claim 17 wherein said sodium chloride-containing food or beverage further contains a compound selected from the group consisting of salty-tasting cationic amino acids and low molecular weight dipeptides.

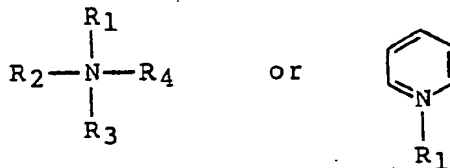
19. A process in accordance with Claim 18 wherein said salty-tasting compound comprises a compound selected from the group consisting of arginine hydrochloride, lysine hydrochloride and lysine-ornithine hydrochloride.

20. A process in accordance with Claim 18 wherein said salty-tasting compound is present in an amount sufficient to produce a 1 to 40 millimolar concentration of said salty-tasting compound in said food or beverage product.

21. A composition having an enhanced salty taste comprising sodium chloride or a food or beverage containing same, a salty-tasting compound selected from the group consisting of cationic amino acids and low molecular weight dipeptides, and salt taste-potentiating amounts of a cationic surfactant having the structure:



where Q is selected from the group comprising:



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wherein N is nitrogen;  $R_1$  is a saturated or unsaturated aliphatic group of at least 11 carbon atoms;  $R_2$ ,  $R_3$  and  $R_4$  are alkyl, aryl, aralkyl or alkoxyalkyl substituents of up to 24 carbon atoms, which substituents are alike or different, or where at least two of which collectively form an aliphatic heterocyclic ring with quaternary nitrogen; X is a mono or polyvalent anion of an acid; m is an integer equal to the valence of the anion X; n is the integer 1; y is 0 or an integer of 1 to 12.

22. A composition in accordance with Claim 21 wherein said salty-tasting compound is selected from the group consisting of arginine hydrochloride, lysine hydrochloride and lysine-ornithine hydrochloride.

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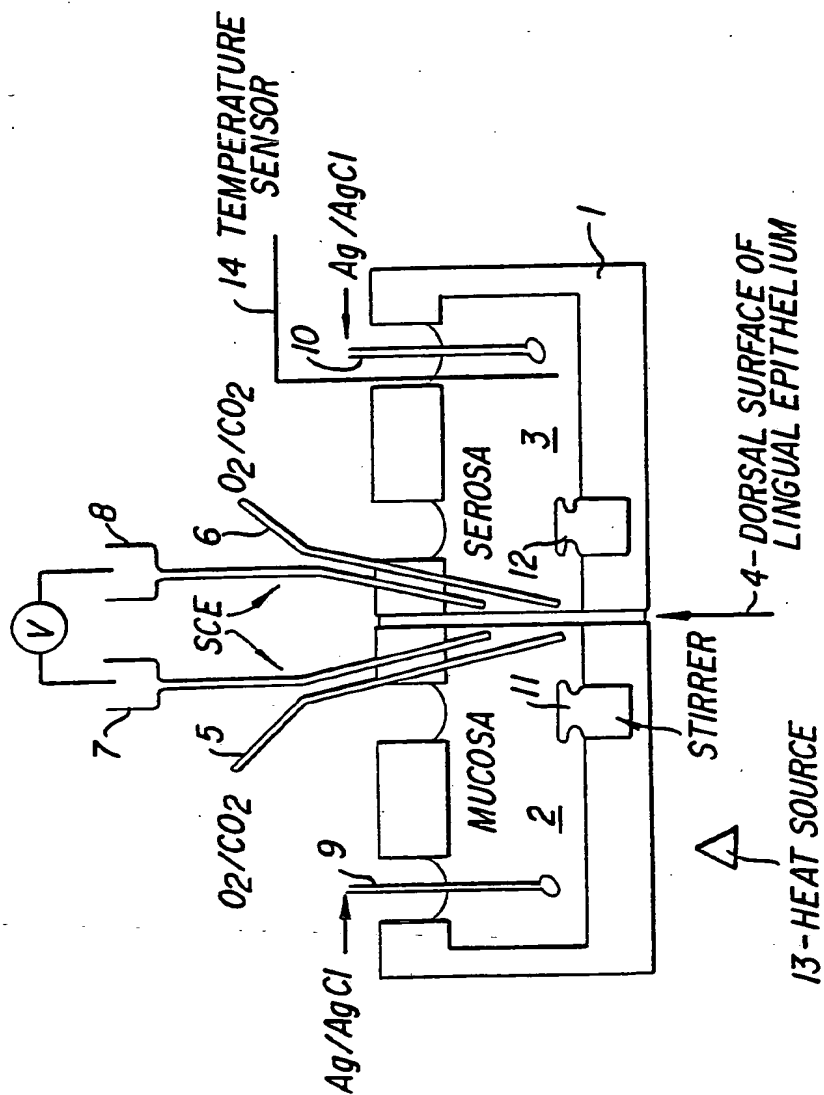


FIG. 1

SUBSTITUTE SHEET

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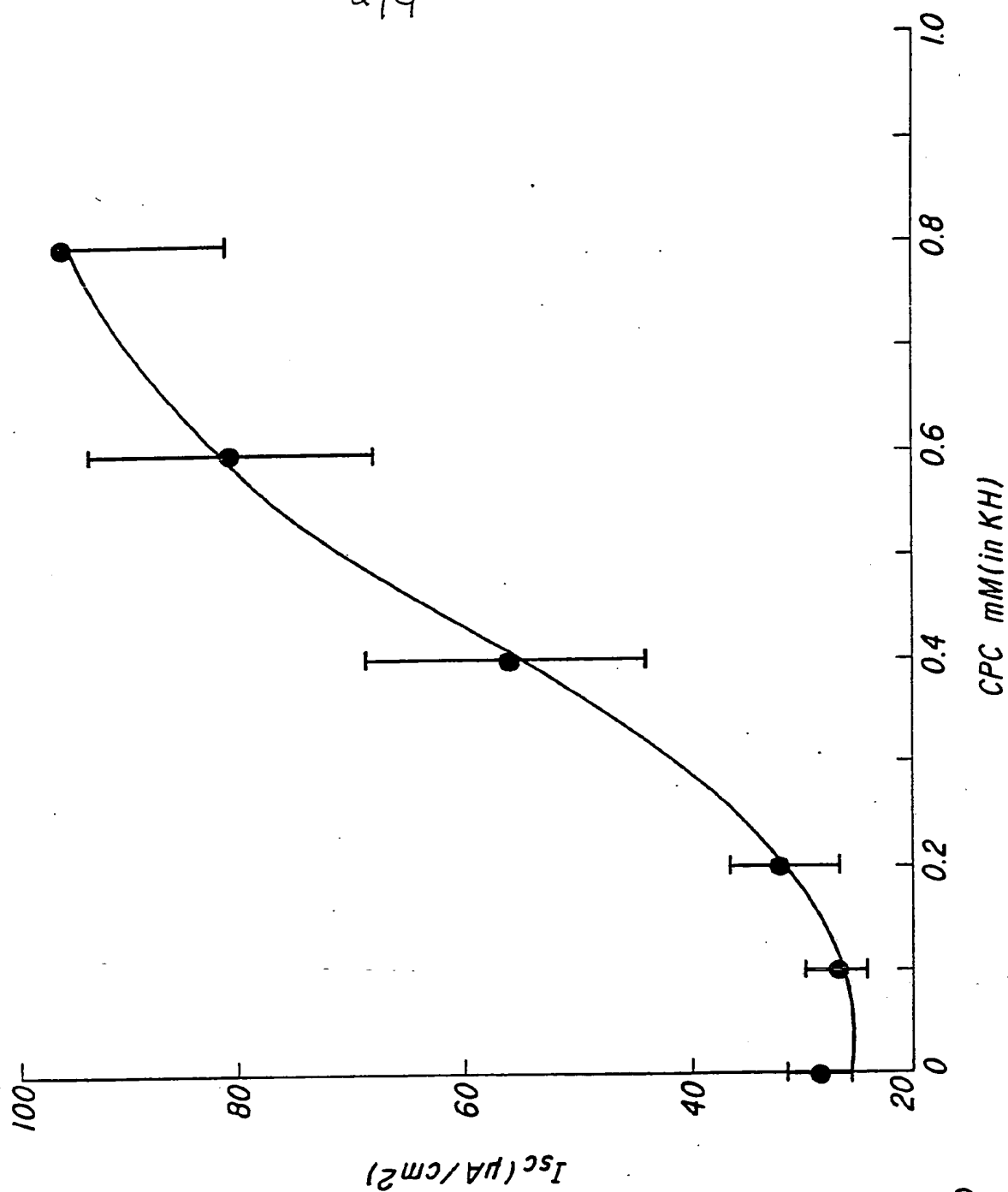
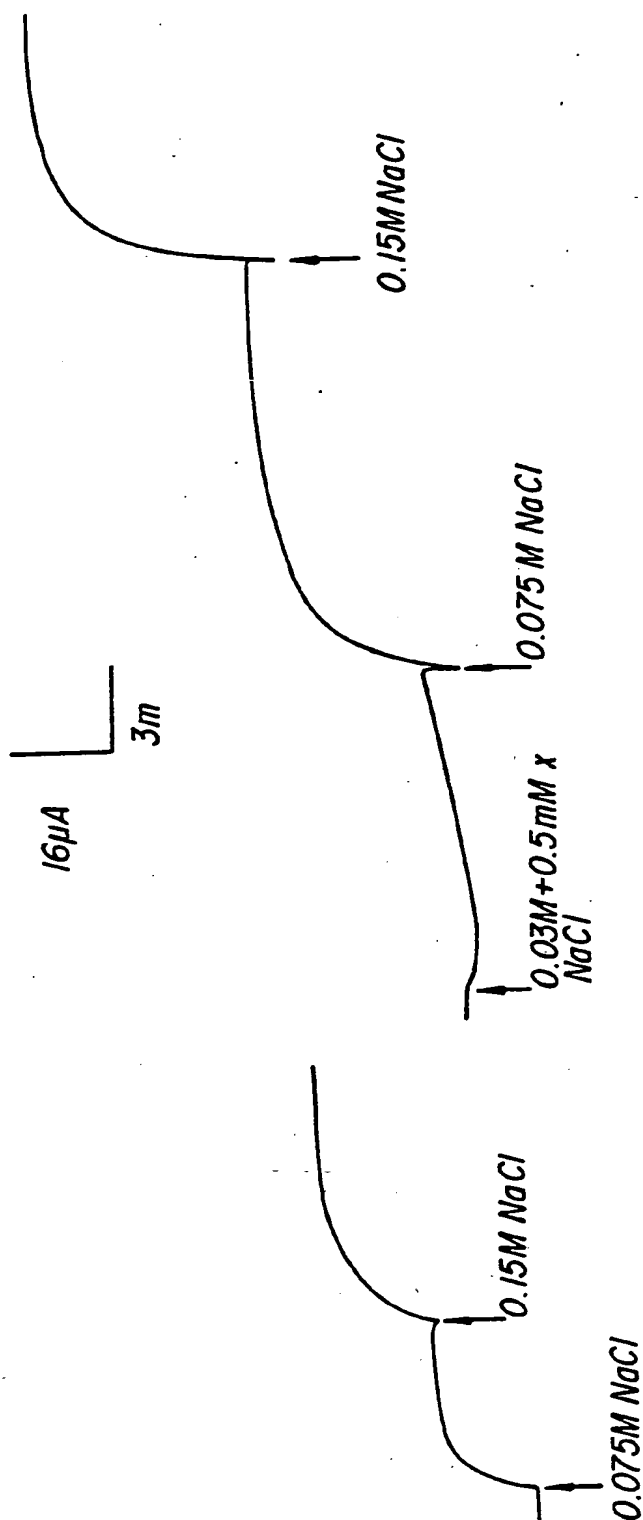


FIG. 2

SUBSTITUTE SHEET

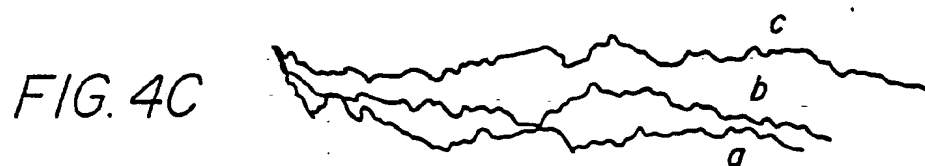
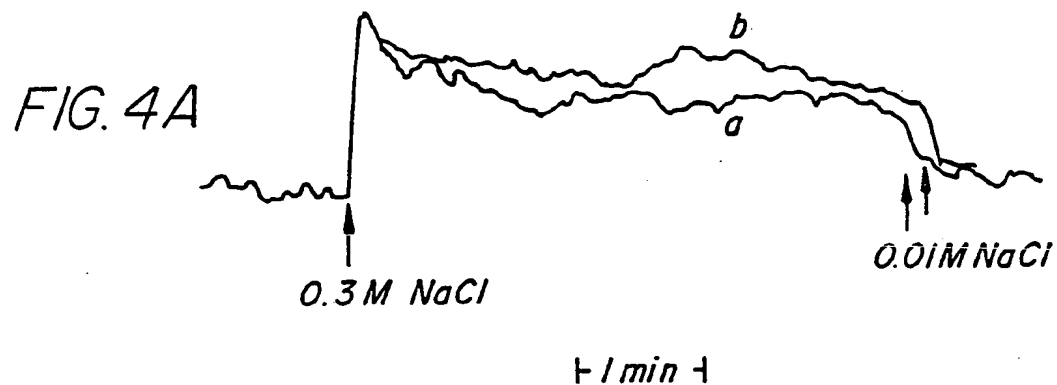
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EFFECT OF 0.5mM CPC ON SALT RESPONSE

FIG. 3

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# INTERNATIONAL SEARCH REPORT

PCT/US88/00467

International Application No.

## I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) <sup>6</sup>

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC(4): A23L 1/237  
U.S. CL. 426/649

## II. FIELDS SEARCHED

Minimum Documentation Searched <sup>7</sup>

Classification System	Classification Symbols
US	426/649

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched <sup>8</sup>

## III. DOCUMENTS CONSIDERED TO BE RELEVANT <sup>9</sup>

Category <sup>*</sup>	Citation of Document, <sup>11</sup> with indication, where appropriate, of the relevant passages <sup>12</sup>	Relevant to Claim No. <sup>13</sup>
X Y	US, A, 2,539,012 (DIAMOND ET AL) 23 January 1951, See Entire Document.	<u>1-22</u> 1-22
Y	JP, A, 57-163464 (Nissian Oil Mills KK) 07 October 1982, See Entire Document.	18-22

\* Special categories of cited documents: <sup>10</sup>

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

## IV. CERTIFICATION

Date of the Actual Completion of the International Search

Date of Mailing of this International Search Report

14 April 1988

24 MAY 1988

International Searching Authority

Signature of Authorized Officer

Joseph M. Goltan

TSA/US